REMARKS

The present paper is presented in response to the **final** office action dated October 16, 2009. This paper is timely filed. In order to ensure consideration of the amendments and remarks presented herein, Applicants are filing this paper with a Request for Continued Examination and accompanying fee.

A. Status of the Claims and Fees

Claims 21-26 and 28-32 were pending in the instant application at the time of examination (claim 27 was previously withdrawn). These claims have been rejected under 35 U.S.C. § 103(a), 35 U.S.C. § 112, first paragraph for lack of written description and 35 U.S.C. § 112, first paragraph for lack of clarity. Applicants respectfully request reconsideration.

B. Rejection under 35 U.S.C. 103(a)

Claims 21-26 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rossow et al., in view of Moormann et al. (J of Virol. 1996 Vol. 70 No 2 pp 673-770).

The Examiner previously maintained the rejection noting that addition of the length of the clone does not change the claim and that the applicant has not explained why the prior art would not produce a full length clone. The Examiner went in the current office action to state that "The claims are drawn to a product" and that the prior art "teaches the need for full length clones". The Examiner dismissed the Applicants previous arguments as non-persuasive because "Applicant is arguing that the prior art does not teach the method steps used to make the recombinant virus as disclosed in the specification but the claims are

drawn to a full length clone, not a method." The Examiner went on to state that "Applicants arguments over the meaning of the limitation would possibly be persuasive if the claims were drawn to method comprising those steps." Applicants respectfully point out that while the instant claims are not method claims *per se*, they are also not straight product claims either but fall into the category of "product-by-process" claims. Referring, for example, to claim 21 as presented in the previous response, it recited "...an infectious RNA molecule encoding a United States strain PRRS virus, said infectious RNA molecule **produced by** transfecting a host cell that is not susceptible to infection by wild-type PRRS virus with a nucleic acid sequence derived from the genome of said United States strain of PRRS virus and ..." This type of language was used in order to claim a product-by-process. However, in order to clarify this further, Applicants have specifically amended the term "produced by" to state "produced by a method comprising the steps of". Applicants believe this specifically clarifies that the claims herein are product-by-process claims that are intended to be limited by the method by which the product is prepared.

In May 2009, the Federal Circuit specifically addressed the patentability of product-by-process claims and admonished that the method steps in such claims for specific limitations of the process claims. The Federal Circuit indicated that product-by-process claims are allowable, legitimate claims in U.S. patent practice noting that "This court does not question at all whether product-by-process claims are legitimate as a matter of form. The legitimacy of this claim form was indeed a relevant issue in the nineteenth century when Ex parte Painter, 1891 C.D. 200, 200-01 (Comm'r Pat. 1891), and some later cases were before the Commissioner of Patents. However, this court need not address that settled issue" (Abbott Laboratories et al. v. Sandoz Inc et al. 566 F.3d 1282 (Fed. Cir. 2009); attached as **Exhibit A**). The Court went on to note that "The patent will issue subject to the

ordinary requirements of patentability. The inventor will not be denied protection. Because the inventor chose to claim the product in terms of its process, however, that definition also governs the enforcement of the bounds of the patent right. This court cannot simply ignore as verbiage the only definition supplied by the inventor." As such, the Federal Circuit pronounced that "In sum, it is both unnecessary and logically unsound to create a rule that the process limitations of a product-by-process claim should not be enforced in some exceptional instance when the structure of the claimed product is unknown and the product can be defined only by reference to a process by which it can be made." The Applicants respectfully request reconsideration of the claims as presented herein in view of this opinion of the Federal Circuit (the slip opinion is attached for the Examiner's convenience) settling the caselaw on product-by-process claims in favor of an interpretation that examination of product claims categorized by the process by which they are made should take into account the process limitations introduced in such claims.

C. Rejection under 35 U.S.C. 112, First Paragraph

Claims 28-32 were rejected under 35 U.S.C. 112, first paragraph because the Applicants presentation of these claims was accompanied by the statement that the claims were supported at pages 18-21 of the specification rather than specific statements as to where the specific cell types and sequence are recited in the specification commensurate in scope with the claims. Applicants provide herein below pin cite support for each of claims 28-32 and respectfully request reconsideration and withdrawal of the rejection.

Claim 28 specifically defines that in the method "said host cells that are not susceptible for infection by wild-type PRRS virus are BHK21 cells." This claim is supported

by the disclosure at page 18, fourth full paragraph under the heading "Infectivity of LV RNA" where it is stated:

> These results indicated that CL2621 cells were not suitable for transfection experiments, whereas the BHK-21 cells (not susceptible to infection with wild-type virus) surprisingly appeared very suitable. Therefore BHK-21 cells were used to test the infectivity of LV RNA.

(excerpt copied from pdf of specification as filed). The next page shows that

> Since the --to a wild-type PRRSV in essence not susceptible-- BHK-21 cells were specifically appropriate for the rescue of virus from intracellular LV RNA and the susceptible CL2621 cells were not, BHK-21 cells were used to test whether RNA transcribed from the genome-length cDNA clones was infectious. Plasmids pABV414/416 were linearized with *Pvu*I

(excerpt copied from pdf of specification as filed). Again at page 21, it is stated that:

> PCR-directed mutagenesis (FIG. 4). When RNA transcribed from the genome-length cDNA clone pABV437 containing the *Pac*I site and pABV442 containing the *Swa*I site was transfected to BHK-21 cells and the supernatant was transferred to porcine alveolar macrophages and CL2621 cells at 24 hours after transfection, infectious virus was produced. The rescued viruses,

(excerpt copied from pdf of specification as filed). These excerpt supports claim 28 in that they show that one of the cells that are not susceptible to infection with wild-type virus that can be used in the production method are BHK-21 cells as claimed in claim 28.

Claim 29 specifically defines that in the method "wherein said cells that are susceptible to PRRS virus infection are porcine alveolar macrophage cells." This claim is supported by the disclosure at page 18, line under the heading "Infectivity of LV RNA" where it is stated:

> LV, preferentially, grows in porcine alveolar macrophages. Thus far, cell line CL2621 or other clones derived from the monkey kidney cell line MA104, are cell lines which have been shown to propagate LV (Benfield *et al.*, 1992; Collins *et al.*, 1992; Kim *et al.*, 1993). Therefore, CL2621 cells were used to determine the optimal conditions for transfection of LV RNA.

This excerpt in addition to the above excerpts from pages 18-21 show that the susceptible cells used were porcine alveolar macrophage cells. Claims 30 and 31 which further define the cells as MA104 cells or CL2621 cells also are supported by the same disclosure.

Claim 32 states that "wherein the utmost 5' end of the viral genome comprises a 10 nucleotide sequence of SEQ ID NO:19" This limitation is expressly supported by the disclosure at page 22 of the specification.

The Examiner notes that "the support found refers to LV, a European strain, not North American virus or the virus deposited as VR-2332" Applicants respectfully traverse what appears to be the underlying assumption of this rejection that the disclosure is limited only to European Strains. At page 4 of the specification it is stated:

PRRSV (Lelystad virus), or "LV", was first isolated in 1991 by Wensvoort *et al.* (1991). It was shown to be the causative agent of a new disease now generally known as a porcine reproductive respiratory syndrome, ("PRRS"). The main symptoms of the disease are respiratory problems in pigs and abortions in sows. Although the major outbreaks, such as observed at first in the US in 1987 and in Europe in 1991, have diminished, this virus still causes economic losses in herds in the US, Europe, and Asia.

PRRSV preferentially grows in alveolar lung macrophages (Wensvoort *et al.*, 1991). A few cell lines, such as CL2621 and other cell lines cloned from the monkey kidney cell line MA-104 (Benfield *et al.*, 1992; Collins *et al.*, 1992; Kim *et al.*, 1993), are also susceptible to the virus. Some well known PRRSV strains are known under accession numbers CNCM I-1102, I-1140, I-1387, I-1388, ECACC V93070108, or ATCC VR 2332, VR 2385, VR 2386, VR 2429, VR 2474, and VR 2402. The genome of PRRSV was completely or partly sequenced (Conzelmann *et al.*, 1993; Meulenberg *et al.*, 1993a, Murthaugh et al, 1995) and encodes, besides the RNA dependent

This list of viruses includes well known strains that are European as well as North American varieties. There is no reason to assume that such viruses will not infect susceptible cells such as monkey kidney cells. Indeed, the attached paper by Kim et al. (JOURNAL OF CLINICAL MICROBIOLOGY, May 2008, p. 1758–1768) (**Exhibit B**) shows that VR 2332 and JA142 PRRSV can be grown in MA104 cell lines (see page 1759). The Applicants respectfully request that the Examiner reconsider the rejection in view of the accepted teachings in the art that PRRSV infects monkey kidney alveolar cells. There is no evidence that a BHK21, which are bovine cells would normally be susceptible to one strain of PRRSV (e.g., VR2332) when they are not susceptible to another strain of PRRS virus, e.g., a European strain. To further corroborate that the present invention can be used in the preparation of full length infectious clones from North American PRRS virus, attached herewith is a publication that appeared after the filing of the present application which clearly shows the generation of a full length genomic clone of North American PRRS virus

rescued in BHK cells (Nielsen et al. JOURNAL OF VIROLOGY. 2003, 3702-3711) (**Exhibit C**).

Applicants respectfully request reconsideration of the rejection in view of the entire teachings of the specification and the post-filing data that show that full length genomic clones can be generated from North American as well as European strains of PRRSV using the co-culturing methods described in the present application.

D. Rejection under 35 U.S.C. 112, Second Paragraph

Claim 23 was rejected under 35 U.S.C. 112, second paragraph because the claim allegedly "requires only a transfected cell comprising the transfected nucleic acid or is the transfected cell part of the newly added intended use clause". Applicants have amended the claim to recite:

> "A co-culture of cells for the production of an infectious RNA molecule comprising a) a culture of cells that are not susceptible to infection by PRRSV wherein the cells are transfected with a DNA sequence of at least 15kb in length encoding an infectious RNA molecule encoding a PRRS virus deposited under ATCC Accession No. VR 2332, which transfected cell is capable of expressing the encoded PRRS virus, said infectious RNA molecule being produced by a host cell that is not susceptible to infection by wild-type PRRS virus and b) a culture of cells that are susceptible to infection by said virus.

Applicants believe this amendment clarifies the claim in that the co-culture is one of a first culture of cells that is transfected with but not susceptible to infection by PRRSV and the second culture of cells is one that is susceptible to infection by PRRSV. Applicants request reconsideration of the claims in view of this amendment.

E. Closing Remarks

Applicants believe the above remarks and amendments overcome the outstanding rejections and Applicants request withdrawal of the rejections and reconsideration of the claims for allowance.

No fees are believed to be due, however, should fees be deemed necessary or should there be an overpayment, the Commissioner is authorized to charge any additional fees or credit any overpayment to the Deposit Account of McAndrews, Held & Malloy, Account No. 13-0017.

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Respectfully submitted,

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